

WHAT IS CLAIMED IS:

1. A system for interrogating a sample using a probe array configured to be responsive to a plurality of particles wherein the probe array generates one or more identifiable signals following interaction with the sample particles and wherein the sample composition is resolved, at least in part, by identifying the signals associated with each constituent probe of the array, the system comprising:

a platform that supports the probe array;

a segmented detector configured to detect at least a portion of the one or more identifiable signals associated with the constituent probes of the probe array wherein the position of each constituent probe and the signal arising therefrom are used to identify the presence or absence of particles contained within the sample wherein the segmented detector comprises a plurality of pixels having a specified dimension and wherein the segmented detector is oriented with respect to the probe array such that the one or more identifiable signals associated with the constituent probes form an optical image of probe array at the segmented detector;

a movement mechanism that provides a relative movement between the platform and the segmented detector wherein the relative movement includes a lateral movement that causes the optical image of the probe array to shift laterally with respect to a normal of the segmented detector and wherein the movement mechanism is capable of such lateral movements in sub-pixel sized steps; and

a processor configured to generate a processed image of the probe array that provides an improved position information of the constituent probes of the probe array, wherein the processor generates the processed image by inducing a plurality of the sub-pixel sized lateral shifts in the image of the probe array with respect to the segmented detector such that the identifiable signals detected at the various lateral positions of the image with respect to the segmented detector are combined to yield a combined signal associated with the combined images such that the combined signal has an effective resolution better than the dimension of the pixel and wherein the combined signal is used to generate the processed image having the improved position information of the constituent probes of the probe array thereby allowing

improved identification of the presence or absence of particles contained within the sample.

2. The system of Claim 1, wherein the movement mechanism comprises a movable stage coupled to the platform and wherein the movable stage is configured to move such that the image moves laterally with respect to an optical axis at the segmented detector and wherein the movable stage is capable of movements that cause the lateral movements of the image at a sub-pixel level.

3. The system of Claim 2, wherein the pixel of the segmented detector has a generally square active area and wherein two perpendicular sides of the square area are respectively generally parallel to X and Y axes of a two dimensional detector coordinate system and wherein the sub-pixel movements of the image comprises sub-pixel movements along the X and Y axes.

4. The system of Claim 3, wherein the magnitude of each sub-pixel movement along the X and Y axes is approximately an integer fraction of the side dimension of the square area.

5. The system of Claim 4, wherein each sub-pixel movement magnitude is approximately  $\frac{1}{2}$  of the side dimension of the square area.

6. The system of Claim 4, wherein each sub-pixel movement magnitude is approximately  $\frac{1}{3}$  of the side dimension of the square area.

7. The system of Claim 1, wherein the platform comprises a bundle of fibers having their tips arranged generally in a planar manner wherein the tips of the fibers form the probe array and wherein the diameter of each fiber defines a feature size to be resolved by the segmented detector.

8. The system of Claim 7, wherein the segmented detector comprises a CCD having a plurality of pixels shaped generally as squares.

9. The system of Claim 8, wherein the pixel square is dimensioned such that the side of the pixel square is greater than approximately  $\frac{1}{3}$  of the diameter of the fiber.

10. The system of Claim 9, wherein the pixel square side is approximately  $21\text{ }\mu\text{m}$  long and the fiber diameter is approximately  $50\text{ }\mu\text{m}$ .

11. The system of Claim 1, wherein the sub-pixel sized shifts of the image relative to the segmented detector allows the processor to estimate what a sub-pixel sized element might output based on the combination of the associated pixels that overlap with the location of the sub-pixel sized element.

12. The system of Claim 11, wherein the sub-pixel sized element is dimensioned according to the magnitudes of the sub-pixel sized shifts.

13. The system of Claim 12, wherein the estimate of the sub-pixel element's output is expressed as  $I = \frac{\sum_i d_i a_i w_i}{W}$ , where  $W = \sum_i a_i w_i$  and wherein  $d_i$  represents the pixel output at the  $i$ -th position,  $a_i$  represents the overlap fraction of the pixel at the  $i$ -th position with the sub-pixel element, and  $w_i$  represents a weight parameter associated with the  $i$ -th position of the pixel.

14. The system of Claim 13, wherein the weight parameter  $a_i$  associated with the  $i$ -th position of the pixel is user defined.

15. The system of Claim 14, wherein the weight parameter  $a_i$  is assigned a constant value of  $1/N$  where  $N$  is the number of pixel positions that overlap with the sub-pixel element.

16. A method for improving the effective resolution of an image of an array of biological probes positioned on an analysis platform and wherein each probe is configured to be responsive to a specific particle having unique identifying characteristics and wherein when the array of probes is exposed to the sample, the probes generate an identifiable signal based on the interaction of the probes with specific particles within the sample based upon the unique identifying characteristics of the specific particle and wherein the identifiable signals from the array of probes are captured by a plurality of pixels of a segmented detector so as to form the image of the array of probes, the method comprising:

inducing a plurality of relative motions between the image of the array of probes and the segmented detector;

capturing the identifiable signals from the array of probes at a plurality of relative positions between the array of probes and the segmented detectors wherein the plurality of relative positions correspond to the plurality of relative motions; and

combining the captured identifiable signals associated with the plurality of relative positions so as to yield a combined image of the probe array that provides an improved position information of the constituent probes of the probe array wherein the combined image has an effective resolution that is better than a dimension representative of the size of an element of the segmented detector and wherein the combined image having the improved position information of the constituent probes of the probe array allows improved identification of the specific particles within the sample.

17. The method of Claim 16, wherein inducing the plurality of relative motions comprises causing the analysis platform to move such that the image of the array of probes moves laterally with respect to the optical axis of the segmented detector.

18. The method of Claim 17, wherein the movement of the analysis platform causes the image to move by a step that is less than the dimension of the pixel of the segmented detector.

19. The method of Claim 18, wherein the image movement step is an integer fraction of the pixel dimension.

20. The method of Claim 19, wherein the pixel of the segmented detector has a generally square active area and wherein two perpendicular sides of the square area are respectively generally parallel to X and Y axes of a two dimensional detector coordinate system and wherein the image movement steps are along the X and Y axes.

21. The method of Claim 16, wherein combining the captured identifiable signals comprises combining outputs of pixels that overlap with a selected area on the segmented detector when the pixels are at the plurality of relative positions with respect to the image.

22. The method of Claim 21, wherein the selected area comprises an area that has sub-pixel dimensions.

23. The method of Claim 22, wherein an output that could result from the sub-

pixel sized selected area is estimated as  $I = \frac{\sum_i d_i a_i w_i}{W}$ , where  $W = \sum_i a_i w_i$  and wherein  $d_i$  represents the pixel output at the  $i$ -th position,  $a_i$  represents the overlap fraction of the pixel at the  $i$ -th position with the selected area, and  $w_i$  represents a weight parameter associated with the  $i$ -th position of the pixel.

24. The method of Claim 23, wherein the weight parameter  $a_i$  associated with the  $i$ -th position of the pixel is user defined.

25. The method of Claim 24, wherein the weight parameter  $a_i$  is assigned a constant value of  $1/N$  where  $N$  is the number of pixel positions that overlap with the selected area.

26. A system for interrogating a sample using a probe array configured to be responsive to a plurality of particles wherein the probe array generates one or more identifiable signals following interaction with the sample particles and wherein the sample composition is resolved, at least in part, by identifying the signals associated with each constituent probe of the array, the system comprising:

a platform that supports the probe array;

a segmented detector configured to detect at least a portion of the one or more identifiable signals associated with the constituent probes of the probe array wherein the position of each constituent probe and the signal arising therefrom are used to identify the presence or absence of particles contained within the sample wherein the segmented detector comprises a plurality of pixels having a specified dimension and wherein the segmented detector is oriented with respect to the probe array such that the one or more identifiable signals associated with the constituent probes form an optical image of probe array at the segmented detector;

a movement mechanism that provides a relative movement between the platform and the segmented detector that causes the optical image of the probe array to move relative to the segmented detector and wherein the movement mechanism is capable of such relative movements in sub-pixel sized values; and

a processor configured to generate a processed image of the probe array that provides an improved position information of the constituent probes of the probe array, wherein the processor generates the processed image by inducing a plurality of the sub-pixel sized relative movements in the image of the probe array with respect to the segmented detector such that the identifiable signals detected at the various relative positions of the image with respect to the segmented detector are combined to yield a combined signal associated with the combined images such that the combined signal has an effective resolution better than the dimension of the pixel and wherein the combined signal is used to generate the processed image having the improved position information of the constituent probes of the probe array thereby allowing improved identification of the presence or absence of particles contained within the sample.

27. The system of Claim 26, wherein the relative movement between the platform and the segmented detector comprises a lateral movement of the optical image of the probe array with respect to a normal of the segmented detector.

28. The system of Claim 27, wherein the movement mechanism comprises a movable stage coupled to the platform and wherein the movable stage is configured to move such that the image moves laterally with respect to an optical axis at the segmented detector and wherein the movable stage is capable of movements that cause the lateral movements of the image at a sub-pixel level.

29. The system of Claim 28, wherein the pixel of the segmented detector has a generally square active area and wherein two perpendicular sides of the square area are respectively generally parallel to X and Y axes of a two dimensional detector coordinate system and wherein the sub-pixel movements of the image comprises sub-pixel movements along the X and Y axes.

30. The system of Claim 29, wherein the magnitude of each sub-pixel movement along the X and Y axes is approximately an integer fraction of the side dimension of the square area.

31. The system of Claim 30, wherein each sub-pixel movement magnitude is approximately  $\frac{1}{2}$  of the side dimension of the square area.

32. The system of Claim 30, wherein each sub-pixel movement magnitude is approximately 1/3 of the side dimension of the square area.

33. The system of Claim 26, wherein the platform comprises a bundle of fibers having their tips arranged generally in a planar manner wherein the tips of the fibers form the probe array and wherein the diameter of each fiber defines a feature size to be resolved by the segmented detector.

34. The system of Claim 33, wherein the segmented detector comprises a CCD having a plurality of pixels shaped generally as squares.

35. The system of Claim 34, wherein the pixel square is dimensioned such that the side of the pixel square is greater than approximately 1/3 of the diameter of the fiber.

36. The system of Claim 35, wherein the pixel square side is approximately 21  $\mu\text{m}$  long and the fiber diameter is approximately 50  $\mu\text{m}$ .

37. The system of Claim 26, wherein the sub-pixel sized relative movement of the image relative to the segmented detector allows the processor to estimate what a sub-pixel sized element might output based on the combination of the associated pixels that overlap with the location of the sub-pixel sized element.

38. The system of Claim 37, wherein the sub-pixel sized element is dimensioned according to the magnitudes of the sub-pixel sized shifts.

39. The system of Claim 38, wherein the estimate of the sub-pixel element's output is expressed as  $I = \frac{\sum_i d_i a_i w_i}{W}$ , where  $W = \sum_i a_i w_i$  and wherein  $d_i$  represents the pixel output at the  $i$ -th position,  $a_i$  represents the overlap fraction of the pixel at the  $i$ -th position with the sub-pixel element, and  $w_i$  represents a weight parameter associated with the  $i$ -th position of the pixel.

40. The system of Claim 39, wherein the weight parameter  $a_i$  associated with the  $i$ -th position of the pixel is user defined.

41. The system of Claim 40, wherein the weight parameter  $a_i$  is assigned a constant value of  $1/N$  where  $N$  is the number of pixel positions that overlap with the sub-pixel element.